

### **III. REMARKS**

#### ***Claim status***

Claims 1, 3-13, 25-27 and 36 are in the case. Claims 2 and 14-23 have been canceled.. Claims 27-36 have been renumbered as claims 26-35. Claim 36 is new. Claims 24, 28-35 (renumbered from 29-36) being drawn to the non-elected process of treatment claims are withdrawn from consideration.

#### ***Claim Objections***

Claim 2 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1.

Claim 2 has been cancelled, thus obviating this ground for objection.

Claim 7 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

The dependence of claim 7 has been amended thus obviating this ground for objection.

#### ***Claim Rejections – 35 USC 103(a)***

Claims 1-13 and 25-27 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Cuny et al. US 6,677,332 in view of Yamamoto et al. US 6,642,257 in that both Cuny and Yamamoto are drawn to piperidinyl compounds having activity in combating pain and are therefore analogous art.

The examiner states that Cuny et al. discloses structurally analogous compounds having pain treating/analgesic activity and exemplifies a structurally analogous species with good activity in example 71.

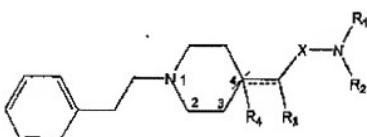
The examiner acknowledges that Cuny et al.'s compound 71 differs from applicants claimed compounds in that in exemplified compound 71 of the prior art the side chain  $-\text{CHR}^3\text{XNR}^1\text{R}^2$  is attached at the 4-position in the presently claimed compound and the prior art compound has the attachment at 3-position of the central piperidinyl ring.

The examiner further states that Yamamoto et al. discloses 4-attachment piperidinyl compounds having similar structure that have good analgesic activity.

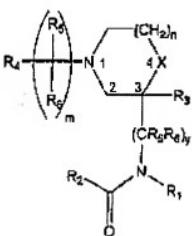
The examiner concludes that one having ordinary skill in the art is deemed to be aware of all the pertinent art in the field and that one skilled in the art would be motivated to modify the compounds of Cuny et al. with a position isomerism because position isomerism has been well recognized in the pharmaceutical art being *prima facie* structural obvious.

Applicants respectfully disagree with the Examiner's position.

First, the examiner acknowledges that compounds of general formula A disclosed by Cuny et al. are different from the compounds of the formula (I) disclosed in the present application in the position of the substitution.



general formula (I) of the present application



general formula A (Cuny et al.)

As recognized by the examiner, the piperidine ring of the compounds according to the present invention is 1,4-disubstituted, whereas the compounds disclosed in Cuny et al. are 1,3-disubstituted.

Cuny et al.'s compounds of general formula A are not limited to piperidine derivatives. In Cuny et al.'s formula A, "X" may be one of 8 different base compounds including members of multiple sub-genuses [where R<sub>2</sub> and R<sub>3</sub> may vary widely]. In the compounds of formula A "X" may stand for, *inter alia*, O, S, SO, SO<sub>2</sub>, NR<sub>2</sub> and NC(O)OR<sub>2</sub> and may contain a 6-membered as well as 7-membered heterocyclic ring systems (n = 1 or 2).

Thus, Cuny et al. discloses a myriad of compounds – none of which are applicant's claimed compounds. In addition, every single one of Cuny et al.'s compounds contains the identical 1, 3 substitution pattern, independently of the ring size and type of heterocycle.

Taken together, the skilled person must therefore come to the conclusion that this fixed 1,3-disubstitution pattern encountered in all of the compounds of Cuny et al. is a prerequisite for the described pharmacological activity.

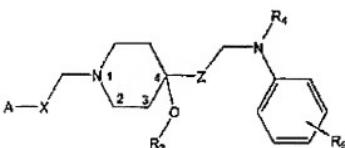
Furthermore, Cuny et al. gives no hint that position isomers of the claimed 1,3-disubstituted compounds of general formula A such as the 1,4- and 1,2-isomers could be worth considering, let alone that these position isomers might show useful

pharmacological properties such as analgesic activity. In particular, there is no suggestion that 1,4-disubstituted position isomers of piperidine containing compounds might also be active.

Consequently, using Cuny et al. as the starting point, the skilled artisan would not arrive at the presently claimed invention, because he would have to choose from multiple different possibilities, namely to choose from numerous substituents, heteroatoms and positions of certain functional groups, without any guidance from Cuny et al. Therefore, Cuny et al. gives no guidance that these significant structural changes could be undertaken, let alone that such structural changes would still lead to compounds with useful pharmacological properties.

Hence, Cuny et al. would not motivate the skilled artisan to 1] select an individual compound from the huge number disclosed by Cuny et al. and 2] then modify the general formula A to arrive at the compounds of the presently claimed invention. Rather, applicant respectfully suggests such a conclusion could only be based on an inadmissible hindsight approach in knowledge of the present invention.

Yamamoto et al. discloses 1,4-disubstituted derivatives that bear a hydroxy or a methoxy group at position 4 of the piperidine ring and which are therefore structurally distinct from the compounds of the present application (cf. Yamamoto et al., col. 66-76, table 6):



General formula (I) (Yamamoto et al.)

Although R3 is defined as hydrogen or methyl, all the disclosed example compounds possess a hydroxy group in position 4 of the piperidine ring. In this

respect it is noted that hydroxy groups are potent H-bond donors that influence the pharmacological activity at receptor binding sites significantly.

Because Yamamoto et al. only discloses compounds bearing a hydroxy group at the particular position 4 of the piperidine ring, any person skilled in the art immediately realizes that such group must be crucial for any pharmacological activity. Accordingly, Yamamoto et al. gives not the slightest hint that the hydroxy group (or methoxy group) can be omitted, let alone that the respective elimination products would still possess any analgesic activity. Again, it is only in knowledge of the present invention that the Examiner could come to the conclusion that the hydroxy group might be omitted.

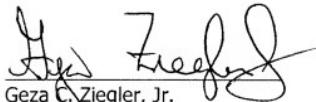
Thus, even if the skilled person would have combined the teaching of both references - even though there was no motivation to do so - he would not have arrived at the presently claimed invention.

Consequently, the presently claimed invention is not only novel, but also involves an inventive step over the cited prior art.

For all of the foregoing reasons, it is respectfully submitted that all of the claims now present in the application are clearly novel and patentable over the prior art of record, and are in proper form for allowance. Accordingly, favorable reconsideration and allowance is respectfully requested. Should any unresolved issues remain, the Examiner is invited to call Applicants' attorney at the telephone number indicated below.

The Commissioner is hereby authorized to charge payment for the two month extension of time (\$450) and the additional dependent claim (\$50) as well as any other fees associated with this communication or credit any over payment to Deposit Account No. 16-1350.

Respectfully submitted,



Geza Ziegler, Jr.  
Reg. No. 44,004

30 July 2007

Date

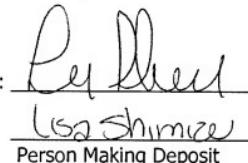
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